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Abstract

There is a well-recognised association between falls and lower urinary tract symptoms (LUTS) in older adults, with estimates of odd ratios for falls in the presence of LUTS ranging between 1.5 and 2.3. Falls and LUTS are both highly prevalent among older people and are both markers of frailty, with significant associated morbidity, mortality, and healthcare resource cost. Despite the recognition of this association, there has been little research to examine the potential causes of this association, and no intervention trial has established if reducing LUTS or urinary incontinence can reduce the risk of falls. In this paper, stemming from a meeting of experts in the field, the current evidence base and hypothesized causal linkage for this association is reviewed and an outline for a potential research agenda to advance the science in the area is forwarded.

Introduction

Urinary incontinence (UI) and lower urinary tract symptoms (LUTS), including urinary urgency, frequency, and nocturia are highly prevalent amongst the general population; this prevalence rises in association with increasing age [1,2]. LUTS and UI are stigmatizing conditions [3], which are often under-reported and under-treated, particularly in older individuals [4,5]. The most common form of UI in older people is urgency urinary incontinence (UUI), urine loss associated with urinary urgency; a sudden, overwhelming desire to void that is difficult to defer [6]. Frequency, urgency and nocturia, the most common LUTS, which are also components of overactive bladder syndrome (OAB) [6], are extremely common in later life; with up to 50% of men and 60% of women aged over 70 years old describing at least one lower urinary tract symptom [1]. The diagnosis of OAB requires the individual to report urinary urgency.

Up to one third of people aged over 65 years, and half of those over 80 years old, will fall in any given year [7]. Falls, defined by the World Health Organisation as “an event which results in a person coming to rest inadvertently on the ground or floor or other lower level” [8] are often recurrent, with around half of people who fall experiencing another within 12 months [9]. Falls negatively affect quality of life, cause individual pain and suffering, lead to functional decline [10], and are associated with significant healthcare resource use. In the UK, 38% of the 816 participants in the Newcastle 85+ Cohort Study had fallen in the previous year, with 10% of those having fallen suffering a fracture at an average cost of £200 per person (2007 prices) [11]. In the USA, there were approximately 24,190 fatal and 3.2 million non-fatal falls among older adults, at a total cost of over US$30billion in 2105 [12]. In Canada it is predicted that by 2031, the annual direct healthcare costs attributable to falls will be C$4.4 billion [13], and in 2004, falls were responsible for 7.3% of all hospital admissions for older people and the annual direct cost of fall-related injuries was estimated at C$2billion [13].

There is a well-recognised association between falls and lower urinary tract symptoms in older adults [14-21]. Older people with urinary urgency or UUI are significantly more likely to fall and sustain injury compared to age-matched controls, with estimates of the odds ratio for falls ranging from 1.5 to 2.3 [15,22,23]. However, the reasons for this association are neither understood nor well-studied. This paper is the result of a meeting of health professionals and researchers with expertise in LUTS in older people, exercise physiology, cognitive processing, rehabilitation and bladder physiology. Here, the current state of the research evidence is reviewed, a theoretical framework to explain the association is proposed, and a research agenda to better explain this phenomenon outlined.

What is known about the association between falls and LUTS?

Brown and colleagues [14] performed a secondary analysis of data from an osteoporosis cohort study, examining a group of 6049 community-dwelling older women using regular self-completed questionnaires sent to all participants every four months. In this cohort, followed for an average of three years, those with at least one weekly urgency urinary incontinence (UUI) episode were more likely to fall (OR 1.26, 95%CI 1.14-1.40) than those without. Weekly UUI was also associated with higher odds of sustaining a non-spinal fracture (hazard ratio 1.34 95%CI 1.06-1.69). In this study, stress incontinence was not associated with higher odds of falling (Odds ratio (OR) 1.06, CI 0.95-1.19) or sustaining a fracture (relative hazard 0.98, CI 0.75-1.28). Analysis of the Concord Health and Ageing in Men Project, a longitudinal study of community-dwelling men in Australia followed 1090 men over a period of 2 years. Here, the presence of urgency incontinence, defined as weekly episodes of UUI, was associated with a higher incidence of falls (OR 2.57 95%CI 1.51 – 4.3) and men with a higher International Prostate Symptom Score storage sub-score, defined a score of 19 and above, had a higher incident rate of falls (incident rate ratio 1.72 (95%CI 1.24-2.38) [24]. A Japanese study of patients with Parkinson's disease found that increased micturition frequency either by day or night was not associated with falls, but that the presence of urinary urgency was strongly associated with a large increase in the odds of falling (OR 5.14 95%CI 1.51-17.48). Only 14% of the falls reported in this study occurred on the way to or from the toilet [25]. There appears to be no association between voiding LUTS and falls in men based upon current published evidence.

A recent systematic review of the association between falls and LUTS in community-dwelling men aged 60 years and over identified six cross-sectional studies and three prospective cohort studies. The identified data were only suitable for qualitative synthesis but urinary incontinence and storage LUTS were consistently shown to have a weak to moderate association with an increased likelihood of falls. None of the identified studies examined potential causes for these associations; the categorisation of continence or not and degree of accounting for confounding variables was inconsistent across the included studies [26]. A small cross-sectional analysis of community dwelling women aged 65 and over in the US examined the association between nocturia, nocturnal enuresis and falls. Neither severity of UI nor severity of nocturia was associated with an increased risk of falls, but there was a statistically significant association between nocturnal enuresis and impairment of physical function and the presence of frailty. However, in the multivariable regression model, which included age, physical function, and the frequency of nocturnal enuresis episodes, only physical function remained as significant risk factor for falls [27].

The use of sedative medications has been identified as a potential risk factor for falls in those with LUTS. In long-term users of benzodiazepines, urinary incontinence and LUTS were an independent risk factor for falls in older adults irrespective of the degree of exposure to these drugs. An exposure-response relationship was observed between the frequency of incontinence and falls, with falls occurring in 17% of participants with incontinence only once weekly, 25% of those with incontinence two to three times per week, 60% of those with incontinence daily, and 58% of those with incontinence more than once per day [28].

There is, therefore, evidence for a reasonably strong association between falls and LUTS/UI in older adults, but the mechanism underlying this is unexplained. Little research has addressed this and additionally, despite calls for such work to be undertaken, no intervention trial has yet been performed to examine if treating LUTS can reduce the risk of falls [29,30].

Potential links and avenues for further study

Rushing to the toilet or slipping in urine

The idea that the reason that people with incontinence are more likely to fall is due to rushing to get to the toilet or by slipping in their own urine following an episode of incontinence has been cited in previous publications as an explanation of the association between LUTS and falls [15,31] without either evidence or clarification. These were reviews, citing no data, and thus there is no evidence in the published literature to suggest that this is the case.

A case-control study in the UK found no temporal association between getting to the toilet and falling, suggesting that a simplistic explanation such as rushing is unlikely to be the underlying link between the two entities [32]. In this study only 6% of participants identified a temporal relationship between their fall and experience of urgency. This is similar to the finding of Sakushima et al [25], which reported 14% of falls related to getting to or from the toilet, but did not examine whether or not those people perceived themselves to be ”rushing”. In addition, there is evidence from continent, middle aged women that the response to a strong desire to void is to slow down, not to speed up or rush [33]. The idea that “rushing” explains the association between urgency and falls should therefore be viewed with caution until evidence supporting this intuitive response is produced. , At present, there is no evidence to support rushing as a link between urgency and falls, and the limited evidence available suggests that rushing is not implicated in the association.

Activity restriction

Lower levels of physical activity have been associated with increased falls [34] and there is evidence that fear of falling is associated with decreased activity in older adults [34,35]. For some people there is consequent avoidance of activity resulting from the fear of falling [36], which in turn further impairs physical ability and increases the risk of future falls [37]. Women with incontinence will often limit their participation in physical activity and sport as a result of their incontinence [38], and recent work found that older women with UI had worse performance on tests of balance and reported more falls than continent, age-matched controls [39]. There is evidence that the presence of urinary incontinence is associated with limitations in activities of daily living [40], and that incontinence in older adults is associated with deconditioning, the development of obesity and a decline in general health [41]. However, some studies have only found reduced levels of physical activity associated with stress, but not urgency incontinence [42]. For example, a French cohort study of 1942 community-dwelling women aged between 75 and 85 used a panel of balance assessments and the International Consultation on Incontinence Questionnaire–Short Form questionnaire (ICIQ-SF) to assess the associations between physical limitation and LUTS. The authors reported a significant deterioration in all the standard mobility and balance test results according to the severity of UI, including timed up and go, standing balance, walking balance, and single leg stand time [43].

Given that deconditioning and reduced physical fitness is associated with an increase in falls risk [44], responding to urinary urgency in a deconditioned older person may, in itself, increase the risk of a subsequent fall. Exercise interventions have been demonstrated to be effective in reducing the frequency of incontinence episodes in nursing home residents [45] and community-dwelling older women [46]. A short-term (8-week) intervention of physiotherapy-delivered training in mobility and toileting skills in non-demented older women living in a care facility resulted in a 37% reduction in the daily urine loss [47]. Likewise there is good evidence that increasing physical activity can decrease falls in older adults living in the community [48], in institutions [49] and in individuals with dementia [50]. A systematic review of cost-effectiveness of falls studies concluded that physical activity, specifically the Otago Exercise programme in those 80 years and older, was one of three cost saving falls prevention strategies [51].

Current evidence tentatively supports a bi-directional relationship between urinary incontinence and activity restriction, with those experiencing incontinence reducing their trips outside the home and those with limited mobility experiencing more incontinence.

FRAILTY, MULTIMORBIDITY, AND POLYPHARMACY

It is undeniable that urinary incontinence, and in particular urgency incontinence, can be considered as a geriatric syndrome and a marker of frailty [52] and, furthermore, frailty is strongly associated with falls [53,54]. Frailty, defined by Fried as "a biologic syndrome of decreased reserve and resistance to stressors, resulting from cumulative declines across multiple physiological systems, and causing vulnerability to adverse outcomes" [55] is not synonymous with multimorbidity, or disability, but rather describes a state of increased vulnerability to adverse outcome. Many tools exist for quantifying and diagnosing frailty [56-58], a detailed discussion of which is beyond the scope of this review.

It is conceivable that no causal link exists between falls and incontinence or LUTS, and that these are both markers of frailty. UI and UUI have been associated with musculoskeletal conditions including low back pain and osteoarthritis in a cross-sectional study of older women in Japan [59]. A retrospective cross sectional study of older patients admitted to hospital in Germany with a fracture found that those with UI were frailer, more dependent, and had higher levels of physical and cognitive impairment than those without UI [60]. Both frailty and LUTS are strongly associated with multimorbidity and polypharmacy [55,61,62], which in turn are influenced by the presence of vascular risk factors [63] and inflammation [64]. A retrospective analysis of drug dispensing data in a Japanese cohort found that polypharmacy was associated with the use of medications known to contribute to urgency [65]. Similarly, a Canadian cross-sectional study identified a strong association (OR 4.9, 95%CI 3.1-7.9) between polypharmacy, defined as 5 or more medications, and the prescription of a medication known to cause LUTS [66]. However, there is little evidence that polypharmacy in the absence of drugs that cause incontinence has an impact on the lower urinary tract.

Several other specific comorbidities are associated with both LUTS and falls. For example, as well as being associated with arterial disease, diabetes mellitus has well documented effects on the lower urinary tract and is associated with impaired bladder emptying and urgency [67], and can cause neuropathies that may predispose to falls including peripheral neuropathy causing gait disturbance and autonomic neuropathy causing postural hypotension [68]. Likewise, Parkinson's disease is commonly associated with both LUTS [69] and falls [70].

These relationships are summarised in figure 1. The observed association between falls and LUTS in older adults may therefore be due to the confounding effect of their multiple common causes. However, given that the epidemiological evidence for this association is overwhelmingly from community-based studies, the majority of available data come from non-frail individuals. Brown et al [71] identified 20% of their cohort as being frail (defined by the investigators based being "weak, unsteady, and fragile") at baseline, and Noguchi et al, although not specifically identifying frailty as a measure at enrolment, described a cohort in which 97% of participants were mobile without the use of a walking aid [24]. A case-control study of nursing home residents in the USA found that those with UI or OAB exhibited higher rates of cognitive impairment, mobility impairment, and higher numbers of comorbidities than those without [72]. It is, therefore, reasonable to suggest that although frailty is a common cause of both falls and LUTS/UI, there are other complex contributors to the association, including the role of cognitive influences and potentially other, as yet unknown, links. The paucity of evidence from frail or institutionalised older people limits the applicability of the current evidence base to this population.

Central control and Cognitive factors

The maintenance of continence is not an innate ability; much like walking, it is a learned skill developed in the early years of life , and once attained, continence is under conscious control [73]. Numerous areas of the brain are involved in the maintenance of continence, with research techniques including brain imaging, functional brain imaging, and evidence from disease-specific studies being used to delineate the complex relationships between them [74]. Functional positron emission scanning in young people shows that the periaqueductal grey matter , pons, and ventral and dorsal portions of the pontine tegmentum are active during bladder filling [75]. Functional magnetic resonance imaging studies in older people suggest that failure of activation in areas of the brain relating to continence, such as the orbitofrontal regions and the insula may lessen the ability to suppress urgency [76]. There is a known association between vascular risk factors and LUTS [63], and the presence of white matter hyperintensities (WMH) within periventricular and subcortical regions of the brain is associated with functional and cognitive impairment, an increased incidence of urinary urgency and detrusor overactivity on cystometry and a difficulty in maintaining continence [77,78]. It has been suggested that changes in the ageing brain, such as the accumulation of white matter hyperintensities, lead to a failure to suppress the physiological sensation of bladder filling , leading to urgency and urgency incontinence [79]. Older adults with vascular dementia are more likely to have LUTS, specifically urgency and urgency incontinence, than those with Alzheimer's disease [80]. those with high WMH burden in the frontal lobes are more likely to have incontinence, more severe incontinence, and higher symptom bother [77].Likewise, the presence of WMH is associated with other geriatric syndromes including cognitive impairment [81] and falls, with data from cross-sectional studies demonstrating that the burden of WMH correlates with frequency of falls [82], and longitudinal data suggesting that the progression of WMH is associated with an increase in the risk of falls in older people over time [83].

The role of executive function in gait and continence

Executive function (EF) can be defined as "a variety of cognitive processes that use and modify information from many cortical sensory systems in the anterior and posterior brain regions to modulate and produce behaviour" [84]. EF covers a broad range of cognitive tasks, divided by Lezak into "volition, planning, purposive action, and action monitoring" [85]. The areas identified by functional brain imaging as being important in the maintenance of continence and the suppression of urgency are also those involved in handling executive function, and a study in community-dwelling women aged 60 found that those with impaired executive function, tested with 5 separate tests, were more likely to have urgency incontinence than other LUTS [86].

Likewise, intact executive function is a necessary component of safe walking [84]. Walking and the avoidance of falling are not automatic tasks; they require continuous cognitive input and control [87,88]. In particular, "successful walking", defined as the ability to get from point to point without falling or fearing falling through instability, is dependent on executive function [84]. Impairment of executive function has been shown to have a negative effect on gait, with associated increased risk of falls; the InCHIANTI study found that cognitively intact older adults who performed poorly on the trail-marking test, a validated test of executive function, had a lower self-selected gait speed when walking over an obstacle course [89].

A key aspect of EF is the ability to dual task, that is, to manage simultaneous tasks which divert attention. Diverted attention is the condition in which performing two tasks simultaneously leads to deterioration in performance of one or both tasks, referred to by some as dual task costs [90]. There are three main categories of explanation proposed for this phenomenon; capacity sharing, a model which suggests that the brain has a finite capacity for global function, and if simultaneous tasks exceed this threshold, performance declines [91]; the bottleneck (or task-switching) model which suggests that individual brain areas can only perform one function at a time, so if competing tasks require the same pathway, a bottleneck occurs, slowing processing and the cross-talk model, which suggests that simultaneous tasks are more difficult if they both require similar sensory input [90]. EF is felt to be predominantly a function of the frontal and prefrontal cortices, those areas involved in the maintenance of continence, but other areas of the brain, including the limbic system and parietal lobes are also involved [84].

There is evidence from continent, middle-aged women that the sensation of a strong desire to void induces changes in gait, including an increase in stride-time variability and reduction in gait velocity [33], changes which are associated with increased falls risk [92]. Performance of a distraction task while attempting voluntary contraction of the urethral and anal sphincters causes a reduction in the strength of the contraction as measured with sphincter electromyography [93]. A Japanese study found that, in a cohort of women attending a clinic with menopausal symptoms, those with urgency incontinence had greater reaction times, as measured with a ruler-drop test, than women with other subtypes of incontinence [94], although no conclusion can be drawn on the direction of effect for this association. Even in healthy, continent young people a strong desire to void has deleterious effects on cognition; a small study using the strong desire to void as a model for pain found that healthy volunteers who were asked to drink fluid until they experienced an "intense urge" to void had significantly worse cognitive performance on tests of detection, visual attention, and working memory compared to both baseline and post-voiding states [95]. In older adults with incontinence, a multicomponent intervention comprising pelvic floor training and video game dancing improved dual-task performance in women aged over 65, with subgroup analysis suggesting that the largest improvement on the n-back test, a measure of dual task ability, was in women with incontinence [96]. In a focus group based study of adults aged 70 years and older, the women involved identified the desire to void as a source of distraction that may affect the performance of other tasks [97].

It can be hypothesised that the sensation of urinary urgency, or the strong desire to void, acts as a source of diverted attention, and that other simultaneous cognitive tasks require dual tasking (at cognitive cost) to complete. Given that dual tasking is a well-recognised cause of gait changes and increased falls risk, it may be that this is one underlying mechanism linking urinary urgency and falls. If urinary urgency is a source of attentional demand, then given that that dual-task training can reduce falls risk under dual task conditions [98-101] there is the potential for novel interventions to address the urgency and linked falls risk.

A MODEL FOR FUTURE RESEARCH

The oft-quoted explanation that urinary urgency causes falls due to rushing to the toilet is an intuitive response, but not supported by the evidence. The temporal relationship between falls and LUTS is far from well-established [25,32], and the response to a desire to void appears to be to slow down, not speed up [33]. The “rushing” hypothesis has not been subjected to systematic examination and should, therefore, no longer be accepted until there is evidence to support this.

There is good evidence that older adults with LUTS are more likely to have lower levels of physical activity, and that people with lower levels of physical activity are more likely to have LUTS, but the direction of this association is unclear. Further research, both epidemiological and interventional, should be considered to delineate and investigate the role of activity restriction on LUTS and the maintenance of continence in older adults and the role of LUTS and incontinence on activity restriction.

Potential relationships and linkages between LUTS and falls risk factors are outlined in figure 2. There are currently many unexplained steps in the relationship between falls and LUTS with a rich research agenda to be explored. The potential role of urgency as a source of attentional demand can be investigated by comparing the performance of various tasks, such as walking or cognitive tests under conditions of no distraction, urinary urgency, and a validated source of diverted attention such as the n-back test. There is a need for further high-quality epidemiological work to disentangle the influences of frailty, multimorbidity and other factors in LUTS and falls, and it remains unknown if current treatments for OAB, including conservative and pharmacological treatments, either reduce or increase the risk of falling in older people [102]. The development of functional brain imaging may provide increasingly sophisticated understanding of the central control of continence, and as our understanding of the underlying physiology of OAB and other LUTS improves, further avenues of study will become apparent. It is clear that WMH are an important common cause of both LUTS and falls, and as such including MRI in studies examining the links between falls and LUTS would be valuable to exclude this factor from analysis.

Despite having a high prevalence of both falls and LUTS, frail and institutionalised older adults are often excluded from research. It is important that researchers consider the needs this population and include them, where possible, in future research.

As Donald Rumsfeld famously told us, the investigation of unknown unknowns is challenging. Clearer data regarding the circumstances of falls in those with LUTS, preferably through robust, prospective data collection, would allow the identification of other potential avenues for study.

There is a rich and unexplored research agenda, and we encourage the development of research projects and programmes to explore these potential links. Does gait change in response to urgency? What changes are observable? Is there a reliable way to induce “urgency” in a gait lab? What underlies this change? Are cognitive factors involved? Are there observable changes to the pelvic floor when walking with and without urgency? Can we ameliorate the associated risk of falls by treating urgency? This is by its nature a multidisciplinary problem and the opportunities for cross-professional collaboration are large.

CONCLUSIONS

There is a clear association between LUTS, in particular nocturia, urinary urgency and urgency incontinence, and falls in older adults, with significant associated morbidity, mortality, and healthcare resource use. It is not clear, however, to what extent this relationship is due to falls and LUTS having a common cause, and how much is due to factors such as dual tasking, activity restriction, and other, as yet unrecognised, mechanisms. There is little evidence supporting the commonly-held belief that this relationship can be explained through rushing to get to a toilet, and there is evidence to support there being at least an element of "common cause"; that both LUTS and UI are common in later life and very common among the frail. Moving forward using the model we outline will facilitate a greater sophistication in understanding of how these factors are linked and identification of novel interventions to test.

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Figure 1: Common causes of falls and LUTS in older adults

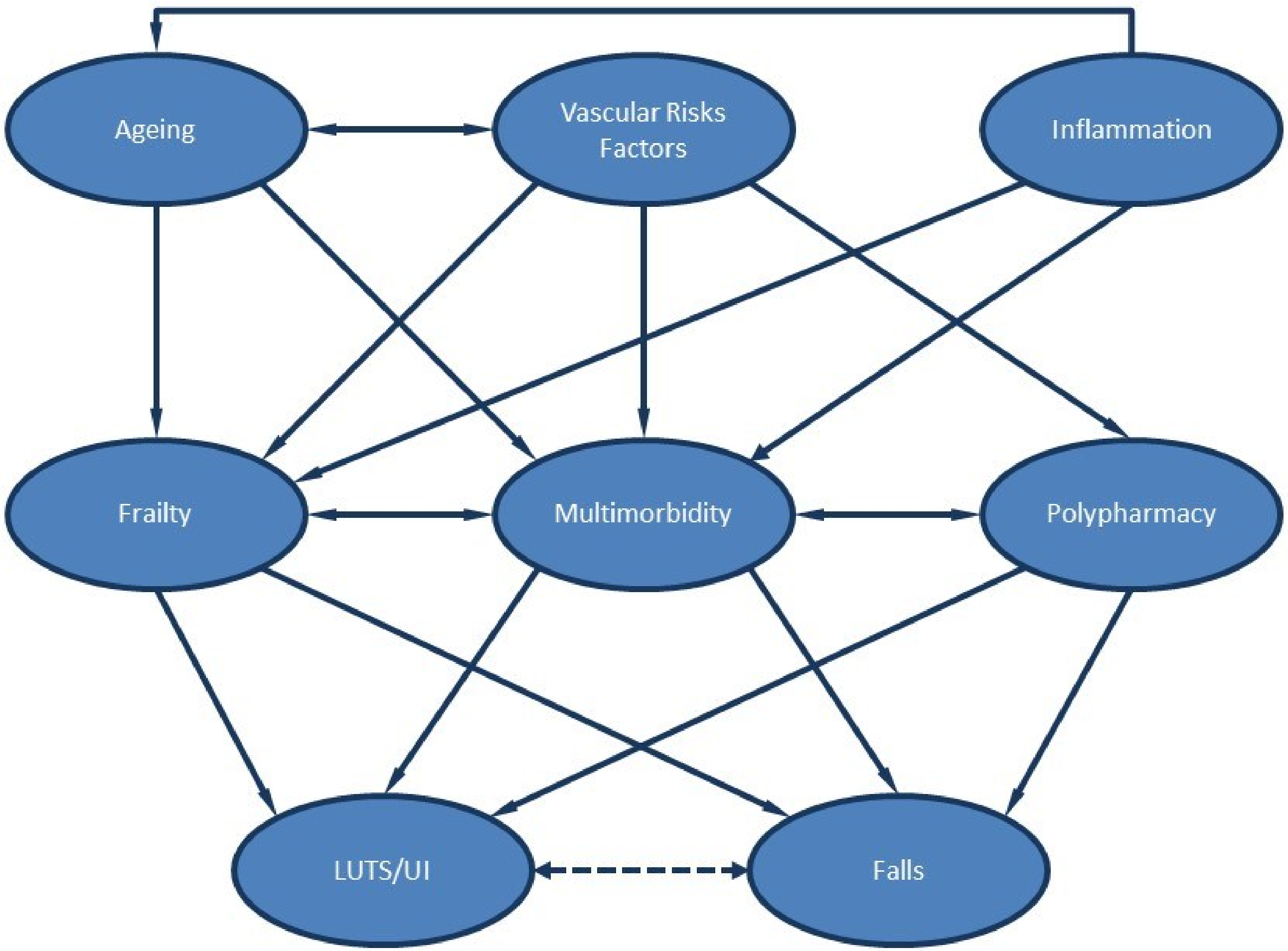

Figure 2: Potential (dashed line), known (solid line), and suggested but likely incorrect (dotted line) links between urgency/LUTS and falls